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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/533,466	03/23/2000	Frank R. Collart	21416/90042	9908

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EXAMINER

MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/533,466	Applicant(s) COLLART ET AL.	
	Examiner Ardin Marschel	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-4,6,7 and 9-15 is/are pending in the application.
- 4a) Of the above claim(s) 9-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4,6 and 7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 2-4,6,7 and 9-15 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 8/5/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 8/5/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have set forth a confusing statement in their REMARKS, filed 8/5/03, in Item III, bridging pages 6 and 7, regarding the allowability of claim 3. No such indication of allowability of claim 3 if rewritten in independent form has been set forth in the previous office action, mailed 2/6/03.

SCOPE OF ENABLEMENT REJECTION

Claims 2-4, 6, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for crystals, crystal complex, molecular complex, or methods of use of a IMPDH crystal, wherein the crystal is set forth with atomic coordinates limited to those in Table 7, does not reasonably provide enablement for any other crystal etc. practice. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue

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experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03. As set forth in the claims previously claims 2-4 and 6 include a scope of crystal practice beyond the Table 7 atomic coordinate disclosure as filed. Claim 6 specifically is inclusive of homologues with significant amino acid differences up to 40% over the Table 7 defined crystal. Claim 7 only requires certain positions be defined by the Protein Data Bank Accession 1ZFJ (apparently derived from Table 7 as cited in the instant specification on page 21, lines 11-12.) leaving other amino acid atomic coordinates to include crystal structures other than those defined by Table 7. These include IMPDH crystal practice which would require the undue experimentation of additional crystallization and atomic coordinate determination. The making of suitable crystals for such crystallization to permit atomic coordinate determination has been noted as undue experimentation due to the Drenth description of the unpredictability of such practices thus making them lacking in enablement. Applicants argue that binding pockets of IMPDH from different bacteria which are similar to the *S. pyogenes* can be

found without undue experimentation. This is an allegation without factual support and is non-persuasive compared to the previously set forth basis for unpredictability set forth in the previous office action. Applicants go on to argue that a high-resolution (1.9 Angstrom) crystal structure of the *S. pyogenes* IMPDH allows catalytic site examination in greater detail than it was possible previously. No prediction or even predictability basis is set forth that such high-resolution is available for other bacterial IMPDH.

NEW SCOPE OF ENABLEMENT REJECTION

It is noted that instant claims 6 and 7 have been amended to refer to atomic coordinates in Accession Number 1ZFJ. This Accession Number 1ZFJ is described on page 11 of the REMARKS, filed 8/5/03, as giving the full IMPDH amino acid sequence as shown in Exhibit C, submitted 8/5/03. Consideration of said Exhibit C reveals that a count of amino acids comes to 434 amino acids. This directly conflicts with the amino acid count in instant Table 7. In Table 7, as originally filed, the atomic coordinates are listed for amino acids 1 through 492 on pages 38 through 114 of the specification. This amending to replace the Table 7 citation in the claims (492 amino acids in IMPDH) with the Exhibit C sequence of 434 amino acids is a replacement which does not correspond to the full length IMPDH but clearly a subsection. Since the crystal atomic coordinates are apparently determined for the full IMPDH, the lesser segment of 434 amino acids in 1ZFJ shown in Exhibit C lacks the scope of enablement corresponding to the actual crystallized molecules. This is a newly applied lack of scope of enablement rejection which is necessitated by amendment.

SCOPE OF ENABLEMENT REJECTION

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (subject to the above scope of enablement rejection) for methods of developing lead compounds utilizing the IMPDH binding pocket as defined by the amino acids set forth in claims 6 or 7, does not reasonably provide enablement for any other IMPDH binding pocket practice as included in instant claim 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03. Applicants allege that well diffracted crystals are provided to practice binding

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pockets other than those defined by instant claims 6 and 7. No such well diffracted crystal disclosures have been pointed to by applicants as filed. Applicants allege that screening for such crystals is routine experimentation but supply no supporting documents or evidence that the above noted IMPDH high resolution type of crystal can be predictably made for other IMPDH enzymes from other than the one which has resulted in the instant Table 7 atomic coordinates. This is therefore an allegation without factual basis and non-persuasive. Applicants have also supplied two Exhibits regarding 3-D modeling regarding this issue. These Exhibits are confusing as to why they have been supplied regarding the issue of enablement of crystallization of suitable crystals beyond the instant Table 7 defined crystal. Both Exhibits A and B are directed to molecular docking and database screening "after" suitable crystals and corresponding atomic coordinates are known. Thus, they are non-persuasive and, in fact, unrelated to the predictability of making suitable crystals for use in atomic coordinate determinations.

LACK OF WRITTEN DESCRIPTION REJECTION

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03. Applicants have not argued this rejection but requested explanation for its

basis. In response such an explanation was already set forth in the previous office action, mailed 2/6/03. To summarize this previously set forth explanation, only the atomic coordinates of Table 7 have atomic coordinate written description including defining the binding pocket amino acid atomic coordinates as set forth in certain claims such as claims 6 and 7. Claim 4, however, is not limited to such Table 7 atomic coordinates but includes Non-Table 7 IMPDH binding pocket atomic coordinates none of which have been set forth as filed regarding any such Non-Table 7 atomic coordinates. Besides the Table 7 atomic coordinates, what others have been set forth as filed? None have been found upon reconsideration of the instant specification as filed.

VAGUENESS AND INDEFINITENESS

Claims 2-4, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03. Applicants argue that the title suggestion indicates clarity of what is meant by "bacterial IMPDH". This argument is non-persuasive because this rejection is not based on title wording nor is the title subject to a rejection of this type under 35 U.S.C. 112, second paragraph. Applicants have also argued that bacterial means IMPDH encoded by a bacterial genome to an enzyme present in the bacteria and point to the specification on page 2, lines 1-22, for support. In response, firstly the encoding clarification of what is meant by bacterial IMPDH has not been amended into the claims

thus leaving the previously set forth two conflicting interpretation still available.

Secondly, consideration of said page 2, lines 1-22, citation reveals no specific definition of "bacterial IMPDH". To further make the definition unclear in response to applicants' argument, on said page 2, lines 5-7, consensus regions are described as being conserved between bacteria and eukaryote IMPDH to percentages of 90% and 85% which is much higher than similar sequence comparison percentages permitted for IMPDH in the last two lines of instant claim 6. This similarity between various IMPDH sequences supports this rejection because bacterial IMPDH sequence may be present in both of the kingdoms of bacteria and eukaryotes as stated on said page 2 of the instant specification as filed.

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03, regarding unclarity as to numbering of amino acids in IMPDH. Applicants only argue this rejection basis in their REMARKS on page 11, filed 8/5/03, in section X., Summary and Conclusion. It has been noted above that Exhibit C, stated as corresponding to Accession Number 1ZFJ, appears to have far fewer amino acids than Table 7, which apparently was the numbering meant for the amino acids in the claims. The amending therefore to cite Accession Number 1ZFJ instead of Table 7 with far fewer amino acids further confuses what numbering is meant for the specific amino acids cited in claims 6 and 7. The basis for this rejection directed to Accession Number 1ZFJ is necessitated by amendment.

PRIOR ART REJECTIONS

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 4 is rejected under 35 U.S.C. 102(b) and (e)(2) as being anticipated by either of Wilson et al. (P/N 6,128,582) or Sintchak et al. [Cell 85:921 (1996)].

This rejection is reiterated and maintained from the previous office action, mailed 2/6/03. Applicants argue firstly that Sintchak et al. does not teach a *S. pyogenes* IMPDH due to only a 35% identity of sequence comparison. In response there is no sequence identity limitation in instant claim 4 thus making this argument non-persuasive due to not being directed to the actually claimed invention. Only bacterial IMPDH is required for the practice of instant claim 4 which is anticipated in the reference due to bacterial host grown IMPDH due to the unclear instant claim 4 wording as noted above regarding the rejection under 35 U.S.C. 112, second paragraph. Thus, this anticipation rejection of instant claim 4 based on Sinchak et al. is maintained.

Applicants then argue regarding Wilson et al. again regarding percent identity. In response again there is no identity limitation in claim 4 corresponding to the argument which is therefore non-persuasive. Also, similar to Sintchak et al., bacterial IMPDH is described in Wilson et al. due to the above noted unclarity present in instant claim 4

wording as noted above regarding the rejection under 35 U.S.C. 112, second paragraph. Thus, this anticipation rejection of instant claim 4 based on Wilson et al. is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whitby et al. [Biochemistry 36:10666 (1997)], taken in view of Wilson et al. (P/N 6,128,582).

This rejection is maintained and reiterated from the previous office action, mailed 2/6/03. Applicants argue this rejection regarding percent identity which is a non-persuasive argument, as also noted above, due to a lack of any such percent identity limitation in instant claim 4. Also, similar to the above anticipation rejections, bacterial IMPDH is described in the references due to the above noted unclarity present in instant claim 4 wording as noted above regarding the rejection under 35 U.S.C. 112, second paragraph. Applicants argue that there was no motivation to combine the above references previously set forth. In response this ignores the equivalent enzyme

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motivation to combine set forth in the previous office action which still is deemed to be proper motivation. Thus, this argument is non-persuasive due to not being directed to the specific basis for this rejection regarding motivation. Applicants then allege that an inhibitor resulting from Whitby et al. would inhibit a mammalian host, but do not indicate such as host nor any such inhibitory practice in Whitby et al. This allegation therefore is without factual basis and non-persuasive.

INFORMALITIES

The disclosure is objected to because of the following informalities:

The objection to page 4, lines 30-31, is maintained. Applicants willingness to amend the "?????" to "?" is acknowledged and requested to be carried out to remove this objection.

Appropriate correction is required.

No claim is allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

This application contains claims 9-15, drawn to an invention nonelected without traverse in Paper No. 6, filed 9/20/00. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.


Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 31, 2003


ARDIN H. MARSCHEL
EXAMINER